

CORRESPONDENCE

Reply: IgG4 antibodies against rodents in laboratory animal workers do not protect against allergic sensitization

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The recent longitudinal study by Krop et al. of laboratory animal workers demonstrates that rat- and mouse-specific IgG₄ antibodies are present before the development of allergy and that the levels remain relatively constant over time. In their study, IgG₄ was not shown to be protective against allergy or symptoms to rats or mice in laboratory animal workers, and on the contrary, workers with mouse sensitization had higher levels of mouse-specific IgG₄.

Several studies examining rat- or mouse-specific IgG have demonstrated an exposure response, whereby IgG antibodies increase with increasing exposure intensity (1–3). Our concern with this study, which was also raised by Krop et al., is that there was not a wide enough exposure range in order for IgG₄ changes to occur and to demonstrate differences in the IgG₄ response over time or for high-dose tolerance to develop. Studies of immunotherapy have demonstrated that higher allergen doses are required for protective antibody responses to develop, and we believe the same is true in the occupational environment as demonstrated in our study of laboratory animal workers (1). Perhaps owing to the restriction in the exposure range, the authors did not identify a tolerant group within the cohort, such as those having high specific IgG₄ with no IgE antibodies, which makes it difficult to examine the role of IgG₄ antibodies without being able to compare sensitized and tolerant individuals.

Another important aspect of the study by Krop et al. was that participants already had an established IgG₄ response at

the beginning of the study, and the mean duration for previous exposure was 10 months. It is therefore likely that the interesting changes in the immune response had already taken place. Immunotherapy studies have demonstrated that the production of allergen-specific IgG₄ antibodies along with their inhibitory activity occurs between 6 and 12 weeks following immunotherapy (4). Therefore, it is possible that the study by Krop et al., although longitudinal in design, missed the early immune response because of the participants having been previously exposed already for some time. Furthermore, the duration of exposure combined with the intensity of exposure may be an important factor in inducing IgG₄ antibodies that have inhibitory effects. The study by Krop et al. was of 2 years duration and may not have allowed for the necessary prolonged exposure to induce such inhibitory antibodies.

Finally, the study includes very few sensitized individuals and thus makes it difficult to fully examine the modified Th2 response or effects of IgG₄ antibodies in such a small population.

Conflict of interest

None.

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